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de Vries, N. K. S.; Erwich, J. J. H. M.; Bos, A. F.

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General movements in the first fourteen days of life in extremely low birth weight (ELBW) infants

N.K.S. de Vries^{a,*}, J.J.H.M. Erwich^b, A.F. Bos^a

^a Department of Pediatrics, Division of Neonatology, Beatrix Children's Hospital, University Medical Centre Groningen, The Netherlands

^b Department of Obstetrics and Gynecology, University Medical Centre Groningen, The Netherlands

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KEYWORDS

Preterm infants;
Optimality scores;
Outcome

Abstract

Objective: To assess the quality of general movements (GMs) in the first fourteen days of life in relation to obstetric and postnatal risk factors and neurodevelopmental outcome in extremely low birth weight (ELBW) infants.

Study design: The GMs of nineteen infants were assessed on days 2, 4, 6, 10 and 14 with Prechtl's method. Additionally, detailed GM assessment produced optimality scores (OSs). GMs and the OSs were related to obstetric and postnatal data and to neurodevelopmental outcome at 18 months. **Results:** GMs and OSs fluctuated substantially during the first fourteen days of life. Most infants had abnormal GMs, especially poor repertoire (PR) GMs. No relation was found between GMs and obstetric factors. Regarding postnatal factors, septicaemia correlated to hypokinesia (H) and artificial ventilation correlated to a lower OS.

Conclusions: Due to physiological disturbances the quality of GM in ELBW infants fluctuates substantially during the first fourteen days of life. Abnormal GMs, especially PR GMs, are mostly seen for the same reason. Septicaemia and artificial ventilation are associated with deterioration of the GMs (lower OSs), and in case of septicaemia also with hypokinesia.

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Abbreviations: BC, blood culture; Ch, chaotic; CoNS, coagulase-negative staphylococcus; CS, cramped synchronized; ELBW, extremely low birth weight; GMH, germinal matrix haemorrhage; GM(s), general movement(s); H, hypokinetic/hypokinesia; NICU, neonatal intensive care unit; Ns, not significant; OS(s), optimality score(s); PR, poor repertoire; PVL, periventricular leucomalacia; SDS, standard deviation score; SGA, small for gestational age; SNAP-PE, score for neonatal acute physiology – perinatal extension.

* Corresponding author. Present address: Department of Pediatrics, Leeuwarden Medical Centre, P.O. Box 888, 8901 BR Leeuwarden, The Netherlands. Tel.: +31 58 2863381; fax: +31 58 2863390.

E-mail address: nathalie.de.vries@znb.nl (N.K.S. de Vries).

1. Introduction

Although extremely low birth weight infants (ELBW) have an increased chance of survival due to the improvement of perinatal care, these infants have a high incidence of abnormal neurological conditions like cerebral palsy and milder neurological disabilities. Unfortunately, we are unable to predict neurodevelopmental outcome accurately directly after birth. Neurodevelopmental outcome can be assessed through neurological examination no earlier than from the end of the first year of life onwards. By using Prechtl's method

of qualitative assessment of general movements (GMs) from videotape, we can assess brain function and predict neurological outcome much earlier, namely in very early infancy (i.e. at preterm age and especially at the age of three to four months post term). This is long before the first signs of spasticity appear [1–4].

GMs are endogenously generated movement patterns in fetuses and infants. Normal GMs are characterized by a large variability in speed, amplitude, force and intensity. The sequence of arm, leg, head, and trunk movements is complex with rotations superimposed on flexion and extension making normal GMs look fluent and elegant. Abnormal GMs appear monotonous with reduced complexity, variability and fluency.

In preterm infants, the results of the assessment of GM quality correlate highly with the presence of brain lesions and neurodevelopmental outcome [3,5–8]. Many preterm infants show qualitatively abnormal GMs during their preterm period. However, the longitudinal approach reveals that the quality of GMs can normalize before, at, or after term age [2,9,10]. Some infants show abnormal GMs consistently after term age which is predictive of an abnormal neurodevelopmental outcome.

Not much is known about general movements in ELBW infants weighing less than 1000 g, since studies have not been performed of groups consisting of ELBW infants only. Especially these ELBW infants are subject to physiological instability during intrauterine and neonatal life that may influence neurological functioning temporarily or permanently. In utero e.g., they may be subjected to chorioamnionitis, maternal medication, and maternal hypertension; during their NICU period they may be subjected to artificial ventilation, cerebral complications, septicaemia, and hyperbilirubinemia. Precht's GM method assesses brain function, and we can hypothesize that GM quality is more often abnormal (be it temporarily or permanently) in ELBW infants during their NICU period, due to the physiological instability. Whether abnormal GMs this early in life are predictive of later neurological deficits is uncertain, although some authors have suggested that this may be the case [9].

The aim of this explorative, prospective and descriptive study was to assess the quality of GMs in the first fourteen days of life of ELBW infants and to examine their relationship to obstetric and postnatal factors, and neurodevelopmental outcome.

2. Patients and methods

2.1. Patients

Between November 2003 and April 2004 nineteen ELBW infants (<1000 g), who had been admitted to the NICU of the Beatrix Children's Hospital in Groningen, The Netherlands, were prospectively enrolled in the study. Infants with major congenital defects were excluded. All parents gave their informed consent. Prenatal and postnatal clinical data were recorded.

2.1.1. General characteristics

The gestational ages ranged from 25 to 31.1 weeks (median 27.0 weeks) and the birth weights ranged from 520 to 995 g (median 835 g). Seven of the nineteen infants were small for

gestational age (SGA) (< -1.3 SDS), and two were born at a local hospital and transported to our NICU postnatally. Two infants died: one on day 3 because of respiratory insufficiency due to immaturity and the other on day 4 because of circulatory insufficiency due to septicaemia.

2.1.2. Obstetrical characteristics

Our study comprised nineteen infants, including one set of twins, and eighteen mothers. Six mothers suffered pre-eclampsia and three also had HELLP. In case of pre-eclampsia, labetalol was the drug mostly used to treat hypertension ($n=5$). Sixteen mothers received corticosteroids to enhance foetal lung maturation in anticipation of preterm delivery. Three mothers did not receive the full course (at least two doses every 24 h 48 h before delivery). Nifedipine ($n=9$) and/or indomethacin ($n=7$) were mostly used for tocolysis in case of spontaneous preterm labour.

Foetal monitoring consisted of monitoring growth, umbilical artery waveform patterns using Doppler ultrasound (normal flow $n=3$, increased pulsatility index $n=3$, absent end-diastolic flow $n=2$, reversed end-diastolic flow $n=4$). In six of the seven growth-restricted infants medial cerebral artery waveforms were assessed, all of them showed brainsparing. The foetal heart rate patterns, monitored by cardiotocography just before delivery, showed a normal pattern ($n=3$), decreased variability ($n=4$) or decelerations ($n=5$). In seven cases no cardiotocograms were available. Two of these infants had been born at a local hospital and five mothers had been admitted with spontaneous labour before 26 weeks' gestational age and a cardiotocogram had not been performed. Ten infants were delivered by Caesarean section and nine were born spontaneously. Blood gas analyses of umbilical cord blood were performed in thirteen patients. The arterial pH ranged from 6.98 to 7.40 (median 7.22).

The net weight of all placentas of infants born in our hospital was 148–380 g (median 208 g). Seven placentas were SGA (<p10). Histological examination of the placentas showed normal placenta ($n=3$), placental bed pathology ($n=8$), signs of infection ($n=5$) or hypoplasia ($n=1$). Birth weight-placental weight ratios were calculated and compared to normal values for gestational age, showing a normal ratio ($n=10$), a decreased ratio ($n=6$) and an increased ratio ($n=1$).

2.1.3. Postnatal characteristics

The median score for neonatal acute physiology – perinatal extension (SNAP-PE), a measure of the clinical condition of the infants during the first 24 h of life, was 35 (range 9–52) [11]. Ten infants had respiratory problems directly after birth necessitating artificial ventilation and surfactant. The use of medication like vasopressors ($N=2$), insulin ($n=2$) and indomethacin ($n=7$) was recorded. Chemical disturbances like acidosis ($pH<7.2$) and the levels of total serum bilirubin at the time of videoing were also recorded.

Brain ultrasound scans were performed at weekly intervals until normalization or stabilization of the degree of abnormality. Of the seventeen surviving infants twelve had normal cerebral ultrasounds. Two infants had a grade 1 GMH on the left and one infant had a grade 3 GMH on both sides, according to Papile et al. [12]. Nine of the nineteen infants showed transient flaring on the brain ultrasounds. Three of

the seventeen surviving infants had periventricular leucomalacia (PVL) grade 1, according to De Vries et al. [13].

2.2. Methods

2.2.1. Recording of spontaneous movements

In all infants one-hour digital video recordings were made on days 2, 4, 6, 10 and 14. A few recordings could not take place because of logistic and patient-related problems. All the recordings were made with the infants lying in the incubator in supine position or on their sides, naked or wearing only a diaper. We took care that the infants could move their limbs and trunks freely. The video camera was located high up at the foot of the incubator. Of all the recordings, at least three parts containing general movements were stored on a digital videodisc and subsequently analyzed.

2.2.2. Analysis of general movements (GMs)

The GMs were analyzed according to Prechtl's method by the authors NV and AB. This method assesses normal and abnormal qualities of GMs on the basis of visual Gestalt perception. Normal GMs are characterized by complexity, variability and fluency. There are three main types of abnormal GMs that apply to the preterm period:

1. Poor repertoire (PR) GMs. The sequence of successive movement components is monotonous and arm, leg, trunk, and head movements do not occur in the normal rich and complex sequence.
2. Cramped synchronized (CS) GMs. The GMs appear rigid and stiff, lack the normal smooth and fluent character and all limb and trunk muscles contract and relax almost simultaneously.
3. Chaotic (Ch) GMs. The movements of all limbs are of large amplitude, they occur chaotically and lack any fluency or smoothness.
4. In case GMs were absent or very short (<3 s) during the 1 h of recording, we scored it as "hypokinetic" (H).

In addition to and following the assessment of the GM quality we assessed the optimality score (OS) according to Prechtl's optimality concept [5,14]. The OS is based on a detailed analysis of GM quality. Eight different aspects of the GMs are distinguished. The first item is "the quality of the GM" and can be scored as normal, variable, and complex (4 points), PR (2 points), Ch (1 point) or CS (1 point). The other seven items are sequence, amplitude, speed, space, rotatory components, onset and offset, and tremulous movement. All can be scored as normal, variable, and complex (2 points) or abnormal (1 point). The highest and therefore the most optimal score is 18; the lowest score is 8.

2.2.3. Follow-up

Two of the nineteen infants died. Two infants were lost to follow-up (one moved abroad and the other did not respond to repeated calls). In the remaining fifteen infants follow-up was performed until a median age of 20 months (12–36 months post term). Follow-up consisted of a paediatric and a Touwen's neurological examination. None of the infants had developed cerebral palsy. Twelve infants had developed normally, while three infants showed motor or speech delay, or both.

2.3. Statistical analysis

Statistical analysis comprised univariate analyses. In case of categorical variables the Fisher's Exact test was used. For non-parametric continuous variables the Mann–Whitney *U* test or the Kruskal–Wallis test was used and for continuous variables we used Pearson's Correlation Coefficient. Differences were considered statistically significant if the probability values (*p* values) were less than 0.05.

3. Results

The results of the quality of GMs of the nineteen ELBW infants and their OSs during the first fourteen days of life are given in Table 1.

3.1. General movements

The quality of GMs changed substantially during the first fourteen days. Almost all GMs were found to be abnormal, of which PR was observed most often.

Five infants sometimes had normal GMs during the first fourteen days of life. In two infants normal GMs were first seen on day 6. Normal GMs during the first fourteen days were not related to any obstetric factor. Of all the postnatal factors GMs were related to the results of the cerebral ultrasounds. We found that none of the nine infants with transient flaring or PVL on the cranial ultrasounds showed

Table 1 The quality of general movements and the optimality scores

Infant	Day 2	Day 4	Day 6	Day 10	Day 14
1				PR (11)	
2		PR (12)	PR (11)*	Ch (8)	PR (13)
3	PR (11)	PR (11)	PR (14)	H (8)*	PR (10)
4	PR (9)	PR (12)*	—	PR (13)	PR (14)
5	Ch (8)	PR (9)	Ch (8)	PR (11)	PR (12)
6	H (8)	PR (9)	PR (10)	H (8)*	PR (9)
7	PR (11)		PR (10)	PR (14)	PR (13)**
8	H (8)	PR (10)	PR (15)	PR (14)	PR (12)**
9	PR (10)				
10	PR (10)	PR (11)			
11	H (8)	PR (10)	PR (10)	PR (10)	PR (10)
12	PR (14)	PR (10)*	H (8)*	PR (11)	PR (11)
13	PR (10)	PR (12)	PR (11)	PR (12)	N (18)
14	PR (8)	PR (13)	N (18)	PR (10)*	H (8)*
15	PR (11)*	PR (14)	N (18)	PR (11)*	PR (12)
16	PR (12)	PR (11)	PR (9)	PR (10)	PR (14)
17	—	H (8)	PR (10)	Ch (8)	PR (9)**
18	PR (11)	PR (12)	PR (11)	N (18)	N (18)
19	PR (9)	PR (9)*	Ch (8)**	N (18)	PR (12)

PR poor repertoire.

N normal.

H hypokinetic.

Ch chaotic.

— could not be assessed due to crying/hiccuping.

(18) optimality score in brackets.

*Positive BC <24 h before/after video recording.

**Positive BC 24–48 h before/after video recording.

normal GMs, whereas five out of ten infants without transient flaring or PVL did have normal GMs. ($p=0.033$).

Hypokinesia was seen in seven infants on eight recordings. Four of these hypokinetic episodes coincided with a positive BC within 24 h of the video recording (see * in Table 1). ($p=0.011$) Of the three infants (6, 8 and 11) found to be hypokinetic on day 2, none of the obstetric data were related to this hypokinesia. Five infants were hypokinetic after day 2. Four of these infants suffered from a sepsis with a positive blood culture (BC) at that time ($p=0.002$). Infant 3 had a coagulase-negative staphylococcus (CoNS) sepsis and needed artificial ventilation. Infant 6, who was still on the ventilator, also had a positive BC with CoNS and *Staphylococcus aureus*. Infant 12 had a CoNS sepsis on day 5 for which she did not need artificial ventilation. Infant 14 suffered severe apnoeas and bradycardia due to CoNS sepsis on day 10 and had been intubated (without medication) for artificial ventilation just before the recording. His GMs changed from normal to PR. On day 14 he lapsed into H. On that day he was extubated and re-intubated. He still suffered from CoNS sepsis (BC still positive) and an open ductus arteriosus for which he was treated with indomethacin. Infant 17, who was hypokinetic on day 4, was not suffering from a sepsis at the time of the video recording. Because of crying and hiccuping it proved impossible to score the first recording made on day 2, so we were unable to determine whether this infant's quality of GMs had changed or not.

Chaotic movements (Ch) were observed five times in four infants. No relationship was found between Ch and obstetric factors. With regards to postnatal factors we found that of the four infants with Ch two had a hyperbilirubinemia of $\geq 240 \mu\text{mol/l}$ on the same day that they showed Ch, while in infants without Ch none were hyperbilirubinemic ($p=0.035$). Although the gestational ages and birth weights of infants with Ch seemed to be higher this was not significant ($p=0.13$ and $p=0.18$ respectively).

No CS movements were seen during the first fourteen days of life.

In three out of the five infants who had normal GMs during the first fourteen days of life, the quality of GM deteriorated to PR. For the changes of GMs in infant 14: see above. Infant 15, whose GMs had also changed from normal to PR on day 10, also suffered apnoeas and bradycardia due to CNS sepsis on that day, but she did not need artificial ventilation. In infant 19 no clinical deterioration or change of treatment was found to explain the change in GM.

3.2. Optimality scores

The OSs changed within individual trajectories. In most infants the OS fluctuated, while in five infants the score gradually increased. Artificial ventilation was the one factor most persistently and significantly related to a lower OS (p values on days 2, 4, 6, 10, and 14 were 0.16, 0.018, 0.14, 0.047, and 0.007 respectively). Of all 80 recordings, a lower optimality score seemed to be related to a positive BC (<24 h) ($p=0.057$). Brain ultrasound results were also related to the OSs. Transient PVE in the first week was related to lower OSs (the p values on days 4 and 6 were 0.014 and 0.07 respectively). A higher serum bilirubin was also related to lower OSs on day 4 ($p=0.011$). Obstetrical factors were not consistently related to the OS.

Throughout the first fourteen days it appeared that on day 14 more factors played a role in the OSs. Infants with a higher gestational age and infants who were SGA had higher OSs ($p=0.022$ and $p=0.021$ respectively).

3.3. GMs and long-term neurodevelopmental outcome

All infants who had normal GMs during the first fourteen days of life had a normal outcome at the median age of 20 months (range 12–36). However, eight infants out of eleven who had not shown normal GMs during the first fourteen days of life also had a normal outcome ($p=\text{ns}$). The OSs were not related to outcome.

4. Discussion

This is the first study on the GMs and OSs of ELBW infants only. Since these infants run the highest risk of developing neurological deficits, it is important to know what factors, be they obstetric or postnatal, relate to brain dysfunction. In the present study these factors could be detected as early as during the first fourteen days of life by assessing brain function with the GM method. We discuss the four major findings of our study, and some (less important) findings that might require further study in the future.

The major new finding of our study was that the quality of GMs and the OSs in ELBW infants fluctuated substantially during the first fourteen days of life. Although it is known that GMs can change in case of an (temporarily) abnormal neurological function, we expected a more stable situation concerning GMs. We offer three possible explanations for this new finding: 1) No study has been performed that studied GMs so frequently directly after birth. Most studies perform video recordings every two or more weeks during preterm life. So we do not know whether fluctuations could also be seen in larger preterm infants or whether they are typical for ELBW infants. 2) No study on GMs has been performed with a group consisting only of ELBW infants. Since many physiological and chemical changes take place in preterm infants after birth that influence brain function (temporarily), one can assume that this is even more so in ELBW infants. This may lead to more fluctuations in the quality of GMs compared to larger preterm infants. 3) Abnormal GMs have a wide spectrum; especially PR GMs. They can range from very poor to almost normal. Since the OS is a more detailed scoring method, one might assume that it is more sensitive in detecting relationships with clinical factors. This might be the case in ELBW infants especially, in whom small changes can affect neurological status.

The second main finding of our study was that PR GMs were observed most frequently. From a previous foetal study we know that the quality of GMs is impaired in complicated pregnancies [15]. From neonatal studies we know that PR GMs are frequently seen among very young infants early in life and that they do not necessarily lead to an abnormal neurological developmental outcome [9,16]. As mentioned above, apparently many physiological and chemical changes take place during this time that influence brain function temporarily and thus result in temporary abnormal GMs.

The third main finding of our study was that septicaemia (with a positive BC within 24 h of the video recording) was

significantly related to hypokinesia. This was even more so in infants who had developed septicaemia after the second day of life. Septicaemia was also related to lower OSs. From a clinical point of view all paediatricians will recognize this sign: A preterm infant who is quiet and less reactive is developing septicaemia. H in relation to septicaemia has not been described previously in the literature, but Bos et al. found a quantitative reduction of GMs in case of septicaemia [17]. Another study reported that GMs become more sluggish (smaller amplitude and slower speed) [18]. In the present study, the quality of GMs was characterized as PR before the onset of septicaemia, whereas the GMs were normal in the studies mentioned [17,18]. We assume that in case of septicaemia GMs deteriorate: normal GMs lapse into PR GMs and PR GMs lapse into H.

The fourth main finding of our study was the persistent significance of a lower OS in case of artificial ventilation throughout the first fourteen days. Artificial ventilation was necessary in our infants because of idiopathic respiratory distress syndrome, septicaemia, persistent ductus arteriosus or other circumstances involving respiratory insufficiency and/or acidosis. These were the most seriously ill infants, which probably explains their lower OS. Only one infant was sedated (morphine) while on the ventilator, so this could not be attributed to the lower OS. These findings may also be explained by the infants' nursing positions. Placing healthy preterm infants in a nest may improve qualitative aspects of GMs [19].

The question may arise whether a reliable assessment is possible in ELBW who are ventilated mechanically and attached to infusion lines. The advantage of the GM method is that it can be carried out without handling the infant at all. Even artificial ventilation, infusion lines and electrodes allow GM assessment as long as the infant can move freely [1,20]. This makes the method especially useful in a NICU setting. Based on our experience we saw no limitations due to tubes or lines. None of our patients, who were ventilated, showed normal movements. Nevertheless, we are convinced that the infants' clinical condition (and thus neurological functions) gave rise to the abnormal GMs, and not the tubes and other accessories.

A limitation of our study is the small sample size. However, the results of our findings were quite consistent with the known literature. Therefore we do not think our results will change much in case of a larger sample.

Some other, but less apparent, findings of our study were:

- a) The relationship between normal GMs and normal cerebral ultrasounds. In our study we observed that normal GMs during the first fourteen days were associated with normal cerebral ultrasounds (no flaring). In other studies on GMs in preterm infants the quality of GMs is also strongly related to periventricular echodensities on brain ultrasounds [5,6].
- b) The association of Ch with a bilirubin count of more than 240 $\mu\text{mol/l}$ (14 mg/dl). The clinical features of bilirubin encephalopathy can be divided into an initial phase with hypotonia and paucity of movements, an intermediate phase with irritability and increased tone and an advanced phase with coma and opisthotonos [21]. We assume that Ch could be due to the intermediate phase of bilirubin encephalopathy. However, since our study was

based on a limited number of infants we should be cautious about this conclusion. Further studies are necessary to clarify the relationship between GMs and hyperbilirubinemia.

- c) The higher OSs on day 14 in infants with a higher gestational age and infants who were SGA. This observation is contrary to the literature. The quality of movement in SGA preterm infants is usually affected more than in adequate for gestational age preterm infants before term. The reason why our SGA infants had a higher OS might be that our study group as a whole had a very high risk of abnormal brain function. Besides, brain function in SGA preterm infants is better due to their higher gestational age. Therefore these infants were less severely ill due to prematurity.
- d) The relationship between GMs and neurodevelopmental outcome. Normal GMs during the first fourteen days of life seem to be associated to a better neurological prognosis. In our study all infants with normal GMs had a normal neurodevelopmental outcome at the age of follow-up. Thus normal GMs during the first days of neonatal life in ELBW infants may be a promising prognostic sign. Other studies on preterm GMs report that most preterm infants show normalization of GMs at or after term. Especially at three to four months post term normal GMs are highly predictive of a normal neurodevelopmental outcome at the age of follow-up. Albers' study is the only study of a group of infants comparable to ours. It also shows a promising prognostic value of GMs from as early as the third week of life in very immature preterm infants in intensive care [9]. They even show a high predictive value of normal movements for normal neurodevelopmental outcome (90–100%). This finding was confirmed by our study in the few infants with normal GMs.

5. Conclusion

Assessing GMs in ELBW infants as early as in the first fourteen days of life is important since GMs reflect brain function and brain dysfunction. GMs and OSs fluctuate substantially in ELBW infants during their first fourteen days due to physiological and chemical disturbances. Most infants displayed abnormal GMs. Septicaemia is related to hypokinesia and lower OSs. Artificial ventilation is related to lower OSs.

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